WE CLAIM:

1. A method for making a hypermutable cell, comprising the step of:

introducing into a mammalian cell a polynucleotide comprising a dominant negative allele of a mismatch repair gene, whereby the cell becomes hypermutable.

2. The method of claim 1 wherein the polynucleotide is introduced by transfection of a suspension of cells *in vitro*.

3. The method of claim 1 wherein the mismatch repair gene is *PMS2*.

4. The method of claim 1 wherein the mismatch repair gene is human *PMS2*.

5. The method of claim 1 wherein the mismatch repair gene is human *MLH1*.

6. The method of claim 1 wherein the mismatch repair gene is human *PMS1*.

7. The method of claim 1 wherein the mismatch repair gene is human *MSH2*.

8. The method of claim 4 wherein the allele comprises a truncation mutation.

9. The method of claim 4 wherein the allele comprises a truncation mutation at codon 134 as shown in SEQ ID NO: 1.

10. The method of claim 9 wherein the truncation mutation is a thymidine at nucleotide 424 of wild-type *PMS2* as shown in SEQ ID NO: 1.

11. The method of claim 1 wherein the polynucleotide is introduced into a fertilized egg of an animal.

12. The method of claim 11 wherein the fertilized egg is subsequently implanted into a pseudo-pregnant female whereby the fertilized egg develops into a mature transgenic animal.

13. The method of claim 12 wherein the mismatch repair gene is *PMS2*.

14. The method of claim 12 wherein the mismatch repair gene is human *PMS2*.

15. The method of claim 12 wherein the mismatch repair gene is human *MLH1*.

16. The method of claim 12 wherein the mismatch repair gene is human *PMS1*.

17. The method of claim 12 wherein the mismatch repair gene is human *MSH2*.

18. The method of claim 14 wherein the allele comprises a truncation mutation.

19. The method of claim 14 wherein the allele comprises a truncation mutation at codon 134 as shown in SEQ ID NO: 1.

20. The method of claim 19 wherein the truncation mutation is a thymidine at nucleotide 424 of wild-type *PMS2* as shown in SEQ ID NO: 1.

21. A homogeneous composition of cultured, hypermutable, mammalian cells which comprise a dominant negative allele of a mismatch repair gene.

22. The isolated hypermutable cell of claim 21 wherein the mismatch repair gene is *PMS2*.

23. The isolated hypermutable cell of claim 21 wherein the mismatch repair gene is human *PMS2*.

24. The isolated hypermutable cell of claim 21 wherein the mismatch repair gene is human *MLH1*.

25. The isolated hypermutable cell of claim 21 wherein the mismatch repair gene is human *PMS1*.

26. The isolated hypermutable cell of claim 21 wherein the mismatch repair gene is human *MSH2*.

27. The isolated hypermutable cell of claim 21 wherein the cells express a protein consisting of the first 133 amino acids of hPMS2.

28. A hypermutable transgenic mammal wherein at least 50% of the cells of the mammal comprise a dominant negative allele of a mismatch repair gene.

29. The hypermutable transgenic animal of claim 28 comprising a protein which consists of the first 133 amino acids of human PMS2.

30. A method for generating a mutation in a gene of interest comprising the steps of:

growing a mammalian cell comprising the gene of interest and a dominant negative allele of a mismatch repair gene, wherein the cell is hypermutable;

testing the cell to determine whether the gene of interest harbors a mutation.

31. The method of claim 30 wherein the step of testing comprises analyzing a nucleotide sequence of the gene of interest.

32. The method of claim 30 wherein the step of testing comprises analyzing mRNA transcribed from the gene of interest.

33. The method of claim 30 wherein the step of testing comprises analyzing a protein encoded by the gene of interest.

34. The method of claim 30 wherein the step of testing comprises analyzing the phenotype of the gene of interest.

35. The method of claim 30 wherein the mammalian cell is made by the process of introducing a polynucleotide comprising a dominant negative allele of a mismatch repair gene into a mammalian cell, whereby the cell becomes hypermutable.

36. The method of claim 35 wherein the step of testing comprises analyzing a nucleotide sequence of the gene of interest.

37. The method of claim 35 wherein the step of testing comprises analyzing mRNA transcribed from the gene of interest.

38. The method of claim 35 wherein the step of testing comprises analyzing a protein encoded by the gene of interest.

39. The method of claim 35 wherein the step of testing comprises analyzing the phenotype of the gene of interest.

40. A method for generating a mutation in a gene of interest comprising the steps of:

growing a mammal comprising the gene of interest and a polynucleotide encoding a dominant negative allele of a mismatch repair gene;

testing the mammal to determine whether the gene of interest harbors a mutation.

41. The method of claim 40 wherein the step of testing comprises analyzing a nucleotide sequence of the gene of interest.

42. The method of claim 40 wherein the step of testing comprises analyzing mRNA transcribed from the gene of interest.

43. The method of claim 40 wherein the step of testing comprises analyzing a protein encoded by the gene of interest.

44. The method of claim 40 wherein the step of testing comprises analyzing the phenotype of the gene of interest.

45. The method of claim 40 wherein the mammal is made by the process of introducing a polynucleotide comprising a dominant negative allele of a mismatch repair gene into a mammal, whereby the mammal becomes hypermutable.

46. The method of claim 45 wherein the step of testing comprises analyzing a nucleotide sequence of the gene of interest.

47. The method of claim 45 wherein the step of testing comprises analyzing mRNA transcribed from the gene of interest.

48. The method of claim 45 wherein the step of testing comprises analyzing a protein encoded by the gene of interest.

49. The method of claim 45 wherein the step of testing comprises analyzing the phenotype of the gene of interest.

50. A hypermutable transgenic mammal made by the method of claim 45.

51. The transgenic mammal of claim 50 wherein the mammal is a primate.

52. The transgenic mammal of claim 50 wherein the mismatch repair gene is *PMS2*.

53. The transgenic mammal of claim 50 wherein the mismatch repair gene is human *PMS2*.

54. The transgenic mammal of claim 50 wherein the mismatch repair gene is human *MLH1*.

55. The transgenic mammal of claim 50 wherein the mismatch repair gene is human *PMS1*.

56. The transgenic mammal of claim 50 wherein the mismatch repair gene is human *MSH2*.

57. The transgenic mammal of claim 50 wherein the allele comprises a truncation mutation.

58. The transgenic mammal of claim 50 wherein the allele comprises a truncation mutation at codon 134 as shown in SEQ ID NO: 1.

59. The transgenic mammal of claim 58 wherein the truncation mutation is a thymidine at nucleotide 424 of wild-type *PMS2* as shown in SEQ ID NO: 1.